Since these patterns were indexed we have learned of an independent single-crystal study by Kjekshus, showing $IrAs_2$ and $IrSb_2$ to be monoclinic (4).

We are indebted to Dr. J. E. Gillott, and to Miss M. McLellan, for assistance in obtaining Guinier and Debye–Scherrer patterns, respectively.

1. R. D. Heyding and L. D. Calvert. Can. J. Chem. **39**, 955 (1961).
2. S. Rundqvist. Acta Chem. Scand. **15**, 451 (1961).
3. N. N. Zhuravlev, G. S. Zhdanov, and R. N. Kuz'min. Soviet Phys. Cryst. **5**, 532 (1961).
4. A. Kjekshus. University of Oslo, Norway. Private communication.

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STEROIDAL 3-CHLORO-3,5-DIENES

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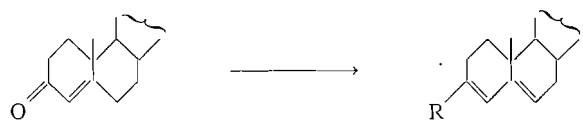
In some cases the modification of the Δ^4-3 ketone moiety (I) of the natural steroidal hormones has led to biologically active analogues, particularly in the anabolic–androgenic field (1, 2).

The 3-enol-ether analogues (3), for instance, (II) R = O-alkyl, of methyltestosterone



I II

were found to be more active, by the oral route, than their parent compound (4).

We chose to modify the Δ^4-3 keto portion of the molecule by forming a 3-chloro-3,5-diene (II, R = Cl), which thus had the same geometry (II) of ring A and B, with concomitant increased stability of the diene system.[1]

Previous examples of steroidal 3-chloro-3,5 dienes were one prepared by Ruzicka by the action of benzoyl chloride at 100° C (5,6) on 4-cholestene-3-one and a 3-chloro-3,5-androstadien-17-one that was described in 1937 by Kuwada (7), but was not completely characterized and was without any mention of its biological activity.

The observation (8) that the action of oxalyl chloride on some Δ^4-3-keto-etianic acids in order to form the corresponding acid chlorides, according to the method of Wilds (9), resulted, in absence of pyridine, in an attack of the Δ^4-3-keto moiety, with the formation of a 3-chloro-3,5-diene,[2] prompted us to employ this reagent to transform a number of steroidal Δ^4-3 ketones into new analogues (II, R = Cl).

The acid-catalyzed reaction proceeds smoothly at room temperature and in most cases is completed in 1 hour in yields of 50–70% of theory.

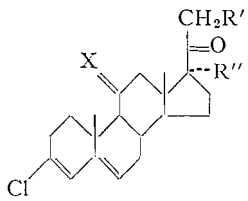
[1]*The 3-enol-ether analogues were assumed to be active "per se" and not as precursors of the conjugated 3-keto steroids by endogenous hydrolysis (4).*

[2]*Reichstein et al. (10) have noted a decrease in the yield of a similar reaction from 83% to 75% when pyridine was omitted. They could isolate minor unidentified by-products which, in our opinion, may well be the corresponding chlorodienes. Oxalic acid is, of course, a product of the reaction and was therefore chosen by us to catalyze our transformations.*

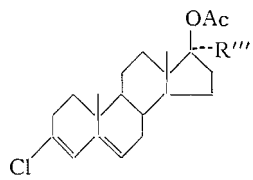
Progesterone, testosterone acetate, methyltestosterone acetate, and cortisone acetate were readily transformed by this method. A hindered alcoholic function (like the 17-hydroxyl group in cortisone) was not affected by the reagent.

The resulting chlorodienes were stable, crystalline substances, with a characteristic ultraviolet absorption at 242 mμ with two shoulders at 236 and 250 mμ and a log ε of 4.4. The infrared absorption in chloroform reveals a single $\Delta^{3,5}$ band at 1621 cm^{-1}. The molecular change in the rotation from the parent Δ^4-3 keto steroid is −850.

The 3-chlorodiene IV, obtained from cortisone, was devoid of appreciable glucocorticoid activity (liver glycogen deposition) but caused sodium excretion; the adduct III from progesterone was inactive in the Clauberg test. 17β-Acetoxy-3-chloro-3,5-androstadiene V (from testosterone acetate) showed a favorable anabolic–androgenic activity ratio (levator ani and seminal vescicles weight test).



III, R′ = R″ = H, X = H_2
IV, R′ = OAc, R″ = OH
X = O



V, R‴ = H
VI, R‴ = CH_3

EXPERIMENTAL[3]

3-Chloro-3,5-pregnadiene-20-one III

A solution of 10 g of progesterone in 100 ml of dry benzene was stirred at room temperature for 2 hours in the presence of 30 cc oxalyl chloride and 0.5 g oxalic acid. The organic solvent was evaporated at reduced pressure and the residue was taken up in ether, washed with $NaHCO_3$ solution, and water. The solvent was dried and evaporated to give crude 3-chloro-3,5-pregnadiene-20-one, 10 g, which was recrystallized from ether. Colorless needles, m.p. 126–128° C, $[\alpha]_D$ −61°, λ_{max} 242 mμ, log ε 4.4. Calc. for $C_{21}H_{29}OCl$ (332.9): C, 75.77; H, 8.78; Cl, 10.65%. Found: C, 75.86; H, 8.76; Cl, 10.56%.

3-Chloro-3,5-androstadiene-17β-ol Acetate V

A quantity of 1 g of testosterone acetate was dissolved in 25 cc dry benzene and stirred with 5 cc oxalyl chloride and 0.1 g oxalic acid for 1 hour. The usual working up gave 0.6 g *17β-acetoxy-3-chloro-3,5-androstadiene*, m.p. 148–152° C, $[\alpha]_D$ −172°, λ_{max} 242 mμ, log ε 4.4. Calc. for $C_{21}H_{29}O_2Cl$ (348.9): C, 72.29; H, 8.38; Cl, 10.16%. Found: C, 72.19; H, 8.30; Cl, 10.10%.

17α-Methyl-3-chloro-3,5-androstadiene-17β-ol Acetate VI

A quantity of 6 g of 17α-methyltestosterone acetate was dissolved in 100 ml dry benzene and stirred with 20 ml of oxalyl chloride and 0.3 g oxalic acid at room temperature for 1½ hours. The reaction mixture was worked up as in the previous examples to give 3.5 g *17α-methyl-17β-acetoxy-3-chloro-3,5-androstadiene*, m.p. 127–128° C after crystallization from methanol, $[\alpha]_D$ −148°, λ_{max} 242 mμ, log ε 4.4. Calc. for $C_{22}H_{31}O_2Cl$ (362.9): C, 72.80; H, 8.61; Cl, 9.77%. Found: C, 73.01; H, 8.45; Cl, 9.90%.

21-Acetoxy-17α-hydroxy-3-chloro-3,5-pregnadiene-11,20-dione IV

A quantity of 3 g of cortisone acetate in 100 ml dry benzene was stirred with 0.4 g oxalic acid and 20 cc oxalyl chloride for 18 hours at room temperature. The usual working up gave needles of *21-acetoxy-17α-hydroxy-3-chloro-3,5-pregnadiene-11,20-dione*, 1.6 g, m.p. 195–197° C from methanol–water, $[\alpha]_D$ ±0, λ_{max} 242 mμ, log ε 4.4. Calc. for $C_{23}H_{29}O_5Cl$ (420.9): C, 65.63; H, 6.94; Cl, 8.42%. Found: C, 65.29; H, 6.76; Cl, 8.43%.

[3]*Melting points were determined in evacuated capillaries and corrected. Rotations measured at 23° C in 1%* $CHCl_3$ *solution.*

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REFERENCES

1. ANON. Brit. Med. J. 1245 (1961).
2. A. ERCOLI and R. GARDI. J. Am. Chem. Soc. **82**, 746 (1960).
3. E. SCHWENK, G. FLEISCHER, and B. WHITMAN. J. Am. Chem. Soc. **60**, 1702 (1938).
4. A. ERCOLI, G. BRUNI, G. FALCONI, R. GARDI, and A. MELI. Endocrinology, **67**, 521 (1960).
5. L. RUZICKA and W. H. FISCHER. Helv. Chim. Acta, **19**, 806, 1371 (1936).
6. W. BERGMANN. J. Org. Chem. **4**, 40, 46 (1939).
7. S. KUWADA, M. MIYASAKI, and S. HOSHIKI. J. Pharm. Soc. Japan, **57**, 234 (1937).
8. R. DEGHENGHI. Unpublished results.
9. A. L. WILDS. J. Am. Chem. Soc. **70**, 2427 (1948); U.S. Patent No. 2,538,611 (Jan. 16, 1951).
10. F. REBER, A. LARDON, and T. REICHSTEIN. Helv. Chim. Acta, **37**, 45 (1954).

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A PHOTOCHEMICAL PREPARATION OF SOME HALOGENATED CYCLOPROPANES

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The photochlorination of cyclopropane was first reported by Gustavson (1). Roberts and Dirstine (2) attempted a flow photochlorination in their investigation of the thermal chlorination of cyclopropane. Using high flow rates, of the order of moles per hour, and a 4:1 ratio of cyclopropane to chlorine, they obtained a yield of monochlorocyclopropane of only 7.6% of the cyclopropane consumed, even with partial recycling of the reaction mixture. Slabey (3), using essentially the same apparatus as Roberts and Dirstine, and similar conditions, but without recycling of the cyclopropane, obtained a yield of about 10%.

In our investigations of the formation and behavior of cycloalkyl radicals in the gas phase, in particular, of the photolysis and mercury-photosensitized decomposition of monohalocyclopropanes, we were led to explore means of preparing these compounds quickly and conveniently. It has been found that cyclopropane can be photochlorinated and photobrominated in a simple flow system without recycling the cyclopropane. In the former case, we were able to obtain yields of monochlorocyclopropane up to 20–30% of the cyclopropane consumed, with flow rates much lower than those used by previous investigators. In the case of photobromination, nitrogen was used as the carrier of bromine, and chlorine served to initiate the photobromination. The yields of monobromocyclopropane were correspondingly lower, usually not exceeding 10% of the cyclopropane consumed. Photobromination, in the absence of chlorine, resulted in the opening of the cyclopropane ring. Attempts to photoiodinate cyclopropane, again with nitrogen as the carrier gas, and chlorine as the initiator, were unsuccessful.

Table I shows some representative results of the photochlorination of cyclopropane. It is seen that the ratio of monochlorocyclopropane to 1,1-dichlorocyclopropane varies directly, while the total yield varies inversely, with the cyclopropane-to-chlorine ratio.